

PRODUCTION OF GP88 BY TUMORIGENIC AND NON-TUMORIGENIC CELLS



FIG.1A

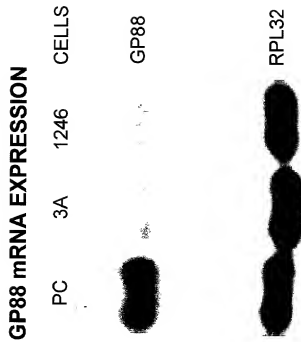


FIG.1B

GP88 mRNA EXPRESSION IN VARIOUS CULTURE CONDITIONS

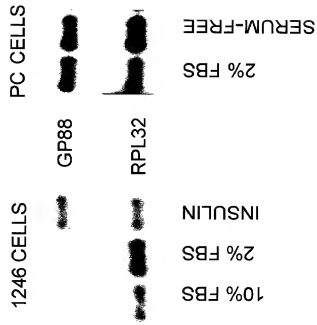


FIG.1C

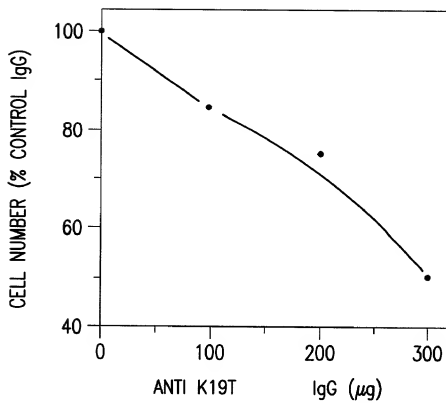


FIG.2

**ABSENCE OF TUMOR FORMATION IN C3H MICE BY INHIBITION OF GP88
EXPRESSION**



GP88 ANTISENSE TRANSFECTED PC CELLS



CONTROL TRANSFECTED PC CELLS

FIG.3

GP88 PROTEIN EXPRESSION IN TUMOR AND SURROUNDING TISSUES

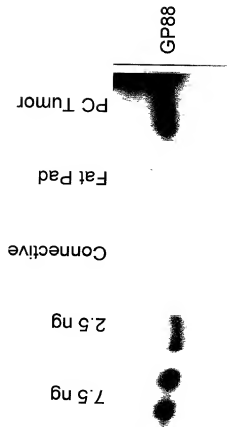


FIG.4

GP88 mRNA EXPRESSION IN ESTROGEN-DEPENDENT AND INDEPENDENT HUMAN MAMMARY CARCINOMA CELLS



FIG.5

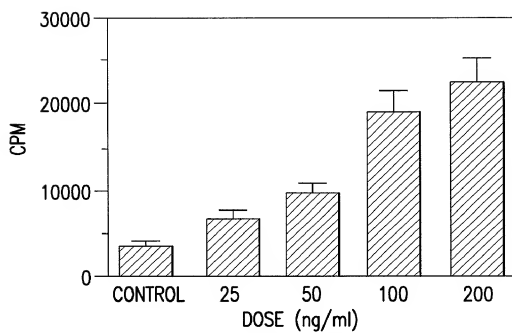


FIG.6A

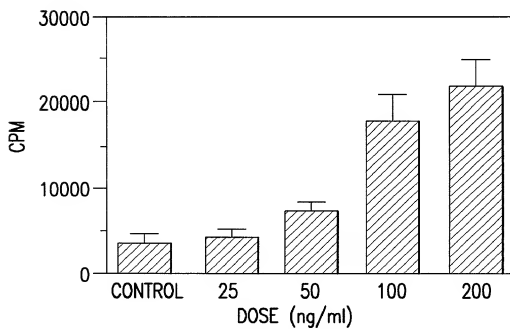


FIG.6B

EXPRESSION OF GP88 IN ANTISENSE AND CONTROL TRANSFECTED PC CELLS



FIG.7

[illegible]FIG. 8A

Mouse GP88 cDNA (continued)

GAT TCT ACC TGC TGT GAG CTA CCC ACT GGG AAG TAT GGC TGC TGT CCA	718
D S T C C E L P T G K Y G C C P	232
ATG CCC AAT GCC ATC TGC TGT TCC GAC CAC CTG CAC TGC TGC CCC CAG	766
M P N A I C C S D H L H C C P Q	248
GAC ACT GTA TGT GAC CTG ATC CAG AGT AAG TGC CTA TCC AAG AAC TAC	814
D T V C D L I Q S K C L S K N Y	264
ACC ACG GAT CTC CTG ACC AAG CTG CCT GGA TAC CCA GTG AAG GAG GTG	862
T T D L L T K L P G Y P V K E V	280
AAG TGC GAC ATG GAG GTG AGC TGC CCT GAA GGA TAT ACC TGC TGC CGC	910
K C D M E V S C P E G Y T C C R	296
CTC AAC ACT GGG GCC TGG GGC TGC TGT CCA TTT GCC AAG GCC GTG TGT	958
L N T G A W G C C P F A K A V C	312
TGT GAG GAT CAC ATT CAT TGC TGC CCG GCA GGG TTT CAG TGT CAC ACA	1006
C E D H I H C C P A G F Q C H T	328
GAG AAA GGA ACC TGC GAA ATG GGT ATC CTC CAA GTA CCC TGG ATG AAG	1054
E K G T C E X G I L Q V P W M <u>K</u>	344
AAG GTC ATA GCC CCC CTC CGC CTG CCA GAC CCA CAG ATC TTG AAG AGT	1102
<u>K V I A P L R L P D P Q I L K S</u>	360
GAT ACA CCT TGT GAT GAC TTC ACT AGG TGT CCT ACA AAC AAT ACC TGC	1150
<u>D T</u> P C D D F T R C P T N N T C	376
TGC AAA CTC AAT TCT GGG GAC TGG GGC TGC TGT CCC ATC CCA GAG GCT	1198
C K L N S G D W G C C P I P E A	392
GTC TGC TGC TCA GAC AAC CAG CAT TGC TGC CCT CAG GGC TTC ACA TGT	1246
V C C S D N Q H C C P Q G F T C	408
CTG GCT CAG GGG TAC TGT CAG AAG GGA GAC ACA ATG GTG GCT GGC CTG	1294
L A Q G Y C Q K G D T M V A G L	424
GAG AAG ATA CCT GCC CGC CAG ACA ACC CCG CTC CAA ATT GGA GAT ATC	1342
E K I P A R Q T T P L Q I G D I	440

FIG.8B

Mouse GP88 cDNA (continued)

GGT TGT GAC CAG CAT ACC AGC TGC CCA GTA GGG CAA ACC TGC TGC CCA	1390
G C D Q H T S C P V G Q T C C P	456
AGC CTC AAG GGA AGT TGG GCC TGC TGC CAG CTG CCC CAT GCT GTG TGC	1438
S L K G S W A C C Q L P H A V C	472
TGT GAG GAC CGG CAG CAC TGT TGC CCG GCC GGG TAC ACC TGC AAC GTG	1486
C E D R Q H C C P A G Y T C N V	488
AAG GCG AGG ACC TGT GAG AAG GAT GTC GAT TTT ATC CAG CCT CCC GTG	1534
K A R T C E K D V D F I Q P P V	504
CTC CTG ACC CTC GGC CCT AAG GTT GGG AAT GTG GAG TGT GGA GAA GGG	1582
L L T L G P K V G N V E C G E G	520
CAT TTC TGC CAT GAT AAC CAG ACC TGT TGT AAA GAC AGT GCA GGA GTC	1630
H F C H D N Q T C C K D S A G V	536
TGG GCC TGC TGT CCC TAC CTA AAG GGT GTC TGC TGT AGA GAT GGA CGT	1678
W A C C P Y L K G V C C R D G R	552
CAC TGT TGC CCC GGT GGC TTC CAC TGT TCA GCC AGG GGA ACC AAG TGT	1726
H C C P G G F H C <u>S A R G T K C</u>	568
TTG CGA AAG AAG ATT CCT CGC TGG GAC ATG TTT TTG AGG GAT CCG GTC	1774
<u>L R K K I P R</u> W D M F L R D P V	584
CCA ACA CCG CTA CTG TAA GGA AGG GCT ACA GAC TTA AGG AAC TCC ACA	1822
P R P L L *	589
GTC CTG GGA ACC CTG TTC CGA GGG TAC CCA CTA CTC AGG CCT CCC TAG	1870
CGC CTC CTC CCC TAA CGT CTC CCC GGC CTA CTC ATC CTG AGT CAC CCT	1918
ATC ACC ATG GGA GGT GGA GCC TCA AAC TAA AAC CTT CTT TTA TGG AAA	1966
GAA GGC TGT GGC CAA AAG CCC CGT ATC AAA CTG CCA TTT CTT CCG GTT	2014
TCT GTG GAC CTT GTG GCC AGG TGC TCT TCC CGA GCC ACA GGT GTT <u>CTG</u>	2062
TGA GCT TGC TTG TGT GTG TGT GCG CGT GTG CGT GTG TTG CTC <u>GAA TAA</u>	2110
<u>AGT</u> TTG TAC GCT TTC TGA AAA AAA AAA	2137

FIG.8C

Nucleotide sequence of human granulin/epithelin precursor (human GP88).
Human Granulin Genbank M75161\$

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[CGcaggcaga ccatgtggac cttggtgagc tgggtggcct taacacgagg gctgggtggct
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gccagctaca gctgctgcg tcccttctg gacaaatggc ccacaacact gagcaggcat
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gtctcaggga cttccagttg ctgcccttc ccagaggccg tggcatgcyg ggatggccat
cactgctgcc cacggggcct cactgcagt gcagacggga gatcctgctt ccaaatgaca
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gatggttcta cctgtctga gctgccagt gggaaagtatg gctgctgccc aatgcccaac
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acctgctgcc aactcacgtc tggggagtgg ggctgctgtc caatcccaga ggctgtctgc
tgctcggacc accagcactg ctgccccag cgatacacgt gtgtagctga gggcagtggt
cagcgaggaa gcgagatcgt ggctggactg gagaagatgc ctgcccgcg cggttcctta
tcccacccca gagacatcgg ctgtgaccag cacaccagct gcccggtggg cggaaacctgc
tgcccagacc aggggtgggag ctgggcctgc tgccagttgc cccatgctgt gtgctgcgag
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aaggacgtgg agtgtgggga aggacacttc tgccatgata accagacctg ctgccgagac
aaccgcaggg gctgggcctg ctgtccctac gccaggggcg tctgtgtgcy tgatcggcgc
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gggaggtggg gcctcaatct aaggcccttc cctgtcagaa gggggttgag gcaaaagccc
attacaagct gccatccct cccggtttca gtggaccctg tggccaggtg cttttcccta
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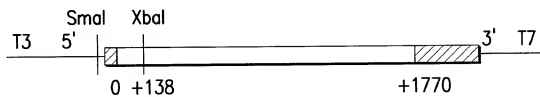
FIG.9A

Amino-acid sequence of human granulin/epithelin precursor (human GP88).

MWTLVSWVALTAGLVAGTRCPDGGFCPVACCLDPGGASYSCCRP
LLDKWPTTLSRHLGGPCQVDAHCSAGHSCIFTVSGTSSCCPFPEAVACGDGHCCPRG
FHC SADGRSCFQRSGNNSVGAIQCPDSQFECPDFSTCCVMVDGSGCCPMPQASCCED
RVHCCPHGAFCDLVHTRCITPTGTHPLAKKLPAQR TNRAVALSSVMCPDARSRC PDG
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HTVGDVKCDMEVSCPDGYTCRLQSGAWGCCPFTQAVCCEDHIHCCPAGFTCDTQKGT
CEQGPHQVPWMEKAPAHLSLPDQALKRDVPCDNVSSCPSSDTCCQLTSGEWGCCPI P
EAVCCSDHQHCCPQRYTCVAEGQCQRGSEIVAGLEKMPARRGSLSHPRDIGCDQHTSC
PVGGTCCPSQGGSWACCQLPHAVCCEDRQHCCPAGYTCNVKARSCEKEVVSQAQATFL
ARSPHVGVKDVECGEGHFCHDNQTCCRDNRQGWACCPYAQGVCCADRRHCCPAGFRCA
RRGTKCLRREAPRWDAPLRDPALRQLL*

FIG.9B

GP88 cDNA CLONE in SK



STRUCTURE OF pCMV₄ EXPRESSION VECTOR

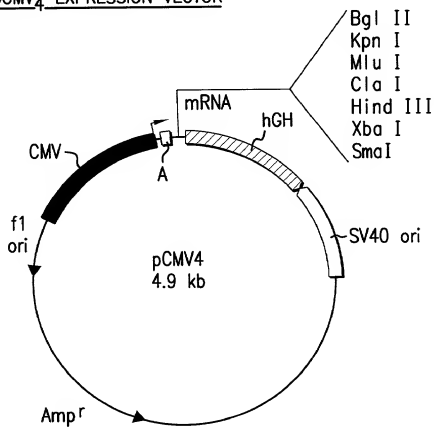


FIG.11

CROSS-LINKING OF ^{125}I -rGP88 TO CCL64 CELLS

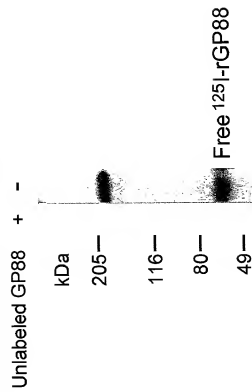


FIG. 12

CROSS-LINKING OF ¹²⁵I-rGP88

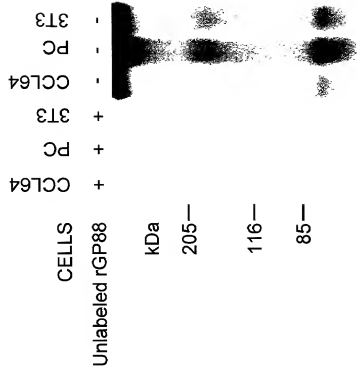


FIG.13

**GP88 EXPRESSION IN NON TUMORIGENIC (MCF 10A)
AND MALIGNANT (MCF 7, MDA-468) HUMAN
MAMMARY EPITHELIAL CELLS**

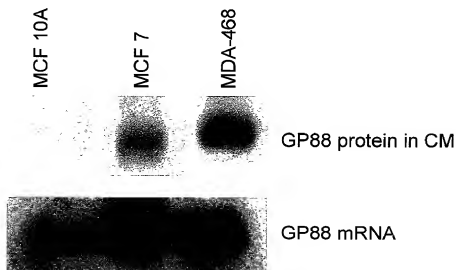


FIG.14

**GP88 EXPRESSION IS INHIBITED BY ANTISENSE GP88
cDNA TRANSFECTION IN HUMAN BREAST
CARCINOMA MDA-468**

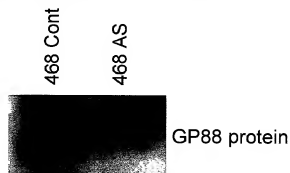


FIG.15

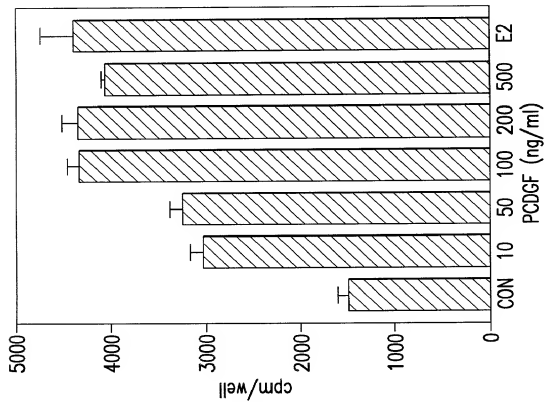


FIG. 16A

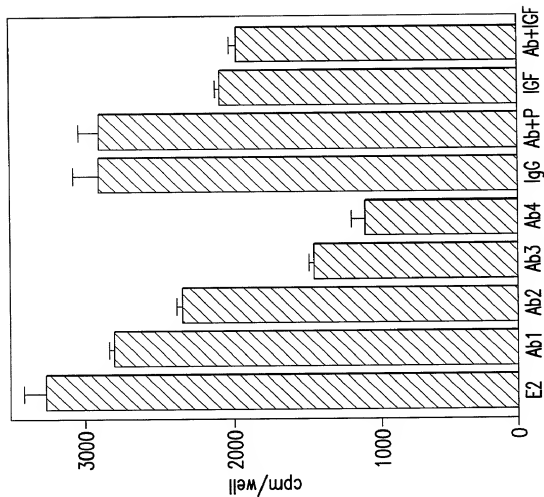


FIG. 16B

AS13
AS22
C



FIG.17A

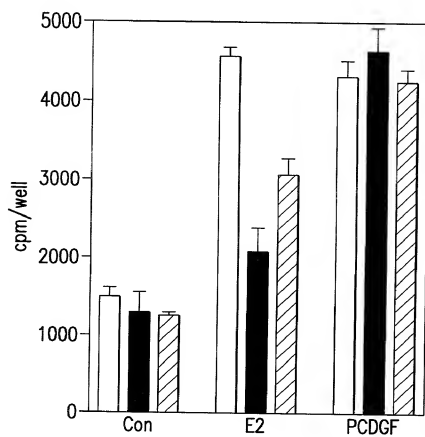


FIG.17B



FIG.18A

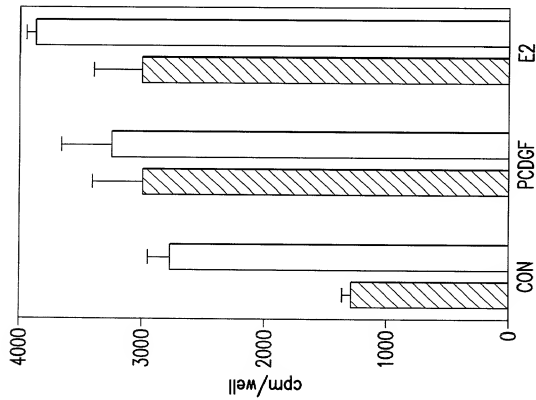


FIG.18B

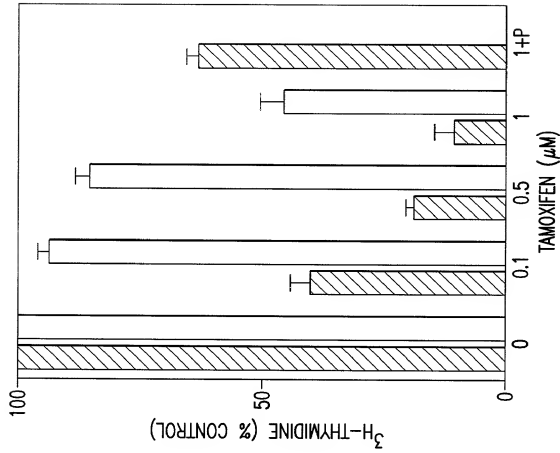


FIG.18C

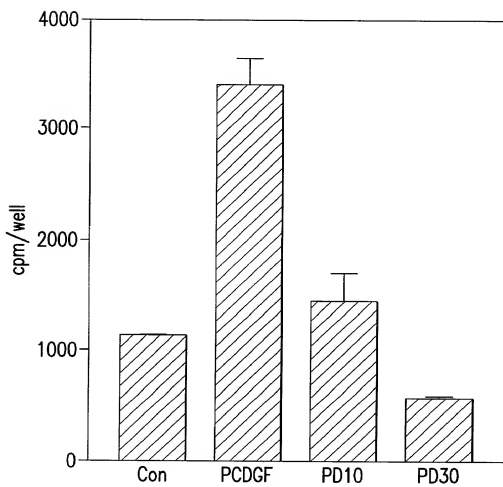


FIG.19A

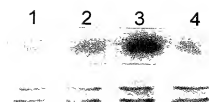


FIG.19B

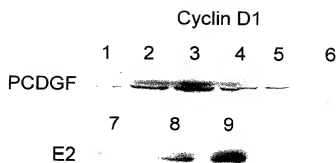


FIG.20A

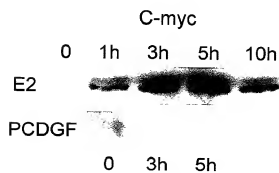
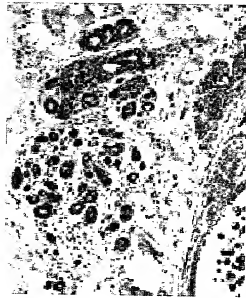
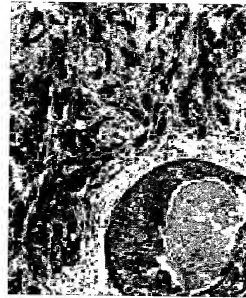


FIG.20B



BENIGN LESION



DUCTAL INVASIVE CARCINOMA

GP88 STAINING WITH ANTI-GP88 ANTIBODY
ON PARAFFIN EMBEDDED BREAST CANCER BIOPSIES
BY IMMUNOHISTOCHEMISTRY (IHC)

FIG.21

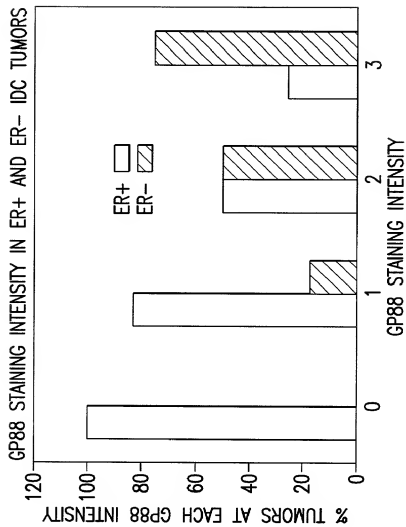


FIG. 22

TAMOXIFEN RESPONSIVENESS OF ER+ IDC TUMORS CLASSIFIED
BY GP88 STAINING INTENSITY

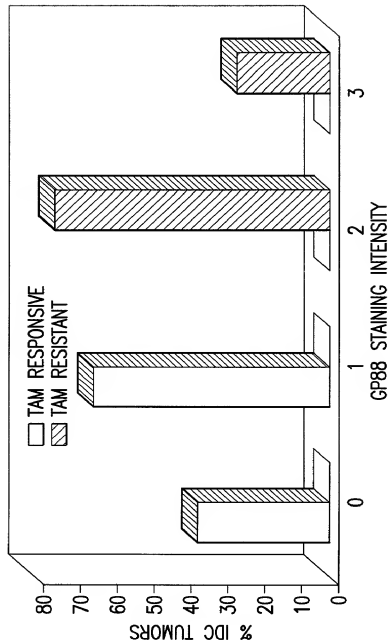


FIG.23